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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,516	02/06/2002	Gillian Rosemary Bullock	4-30755B	4159

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
KIM, JENNIFER M	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
04/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/072,516	BULLOCK ET AL.	
	Examiner	Art Unit	
	Jennifer Kim	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-25,27,28,31,32 and 42* is/are pending in the application.

4a) Of the above claim(s) *15-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25, 27,28,31,32 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/468,663.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed January 10, 2008 have been received and entered into the application.

Action Summary

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 25, 27-28 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Gasparo et al. (WO 95/24901) in view of Wagner et al. (WO 97/49394) of record.

De Gasparo et al. illustrate a composition comprising valsartan (80mg) as an active agent, microcrystalline cellulose (110mg), crospovidone (26.0mg) and magnesium stearate. (page 6, Example 1). The amount of the crospovidone utilized in the illustrated composition is within Applicant's amount set forth in claim 27. That is the

crospovidone contained in the illustrated composition is less than 13% by weight. The ratio of microcrystalline cellulose to crospovidone utilized in the illustrated composition is within Applicants' weight ratio set forth in claim 28. The amount of microcrystalline cellulose in the illustration composition encompass Applicants' amount set forth in claim 25. That is the content of microcrystalline cellulose is more than 30% (i.e. 41% by weight). De Gasparo et al. teach that the dose of the active agent can depend on various factors such as the mode of administration, the species of warm-blooded animal, age and/or individual condition. In normal cases, the approximate daily dose for a patient weighing about 75kg is estimated to be, in the case of oral administration, from approximately 10mg to approximately 250mg. De Gasparo et al. teach that the pharmaceutical compositions preferably comprise an active ingredient (valsartan) from approximately 1% to approximately 60%. (page 4, 5th full paragraph). De Gasparo et al. teach that excipients including silica acid (hydrated silica) can be utilized as a lubricant in the composition. (page 5, lines 7). De Gasparo et al. teach that the composition can be formulated as a unit dose form including tablets. (page 4, 5th full paragraph).

De Gasparo et al. do not expressly teach the tablets are compressed, and the specific ratio of valsartan to microcrystalline cellulose set forth in claim 25, and the amount of microcrystalline cellulose set forth in claim 42.

Wagner et al. teach that valsartan tablet can be prepared by compression method. (abstract, page 7, 2nd full paragraph, page 14, lines 16-17).

It would have been obvious to one of ordinary skill in the art to modify the ratio of valsartan and its conventional pharmaceutical excipients such as microcrystalline cellulose because De Gasparo et al. teach that the dose of the active agent can depend on various factors such as the mode of administration, the species of warm-blooded animal, age and/or individual condition. However, in normal case, the approximate daily dose for the patient weight about 75kg is estimated to be in the case of oral administration from approximately 10mg to approximately 250mg. Further, De Gasparo et al. teach that the pharmaceutical compositions preferably comprise from approximately 1% to approximately 60% of valsartan. One would have been motivated to adjust the ratio of valsartan and its pharmaceutical carrier such as microcrystalline cellulose in order to provide the daily dosages that are needed based on the individual weight and their severity of conditions.

The limitation of the tablet as being a "compressed tablet" is obvious because Valsartan formulation is well known in view of Wagner to be formulated using the compression process.

Claims 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Gasparo et al. (WO 95/24901) in view of Wagner et al. as applied to claims 25, 27-28 and 42 above, and further in view of Pool et al. (1998) of record.

De Gasparo et al. and Wagner et al. as applied as before.

De Gasparo et al. and Wagner et al. do not teach the specific amount (320mg) of valsartan set forth in claims 31 and 32.

Pool et al. teach that the integrated analysis demonstrated a clear increase in blood-pressure-lowering efficacy with increasing dose across the range 10 to 320mg valsartan. The data demonstrate that valsartan provides dose-responsive antihypertensive efficacy across the therapeutic dose range with 10, 20, 40, 80, 160 and 320mg. (abstract).

It would have been obvious to one of ordinary skill in the art to optimize the dose of valsartan in De Gasparo et al's formulation to 320mg as taught by Pool et al. because there is clear increase in blood-pressure-lowering efficacy with increasing dose of valsartan as taught by Pool et al. One would have been motivated to increase the dose of valsartan taught by De Gasparo et al. to 320mg in order to achieve an increased therapeutic effect of lowering blood pressure with higher dosage taught by Pool et al. There is a reasonable expectation of successfully treating hypertension with higher dosage of valsartan than De Gasparo et al's amount because Pool et al. demonstrate that there is clear increase in blood pressure lowering efficacy with increased dose of valsartan. With regard to upper limit of valsartan set forth in claim 31 is obvious within skilled in the art because De Gasparo et al. teach the dosage amount of valsartan is easily determined and adjust by person skilled in the art by routine experimentation and with no undue burden. One of ordinary skill in the art would have easily determined upper limit or maximum dosage of valsartan to be employed accordance of a patient to be treated based on his medical condition/history.

For these reasons the claimed subject matter is deemed to fail to patentably distinguish over the state of the art as represented by the cited references. The claims are therefore properly rejected under 35 U.S.C. 103.

None of the claims are allowed.

Response to Arguments

Applicants' arguments filed January 10, 2008 have been fully considered but they are not persuasive. Applicants argue that Wagner et al. discloses tablets comprising valsartan and microcrystalline cellulose in the amount of 10 to 45% by weight, preferably 20% to 30% by weight and 15% to 25% by weight and Wagner et al. do not teach, suggest or motivate one skilled in the art to increase the content of microcrystalline cellulose to more than 30% or to reduce the ratio of valsartan to microcrystalline cellulose between 2:1. This is not found persuasive because disclosed examples and preferred embodiments do not constitute as no teaching, suggestion or motivation from employing a broader disclosure or nonpreferred embodiments. In this case, De Gasparo et al. illustrate a composition comprising valsartan (80mg) as an active agent, microcrystalline cellulose (110mg), crospovidone (26.0mg) and magnesium stearate. (page 6, Example 1). The amount of microcrystalline cellulose in the illustration composition encompass Applicants amount set forth in claim 25. That is the content of microcrystalline cellulose is more than 30% (i.e. 41% by weight).

Further, De Gasparo et al. teach that the dose of the active agent can depend on various factors such as the mode of administration, the species of warm-blooded animal, age and/or individual condition. In normal cases, the approximate daily dose for a patient weighing about 75kg is estimated to be, in the case of oral administration, from approximately 10mg to approximately 250mg. De Gasparo et al. teach that the pharmaceutical compositions preferably comprise from approximately 1% to approximately 60% of valsartan. (page 4, 5th full paragraph). Therefore, it would have been obvious to one of ordinary skill in the art to modify the ratio of valsartan and its pharmaceutical excipients such as microcrystalline cellulose in order to provide customize dose necessary for the individual patients to be treated. As anyone of ordinary skill in the art will appreciate, De Gasparo et al's preferred dosages and ratio's are merely exemplary and serve as useful guideposts for the physician. There are, however, many reasons for varying dosages, including by orders of magnitude; for instance, an extremely heavy patient or one having an unusually severe conditions would require a correspondingly higher dosage. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 571-272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/
Primary Examiner, Art Unit 1617

Jmk
March 25, 2008